

12/20/03  
Application No.: 09/982,892  
Amendment Dated 29 December 2003  
Response to Office Action of 27 June 2003

### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

#### Listing of Claims

1 (Original): A bioconjugate of a bioactive agent and an organocobalt complex wherein the bioactive agent is covalently conjugated to the cobalt atom <sup>of the organocobalt complex</sup> through a non-reactive atom in the bioactive agent molecule, wherein said bioactive agent is selected from the group consisting of a peptide, a peptide analogue, a protein, a protein analogue, a nucleic acid and a nucleic acid analogue.

2 (Original): The bioconjugate of claim 1, wherein said non-reactive atom is selected from the group consisting of a carbon atom, a nitrogen atom, an oxygen atom, a sulfur atom, a selenium atom or a silicon atom.

3 (Original): The bioconjugate of claim 1, wherein said non-reactive atom is a carbon atom.

4 (Original): The bioconjugate of claim 1, wherein the non-reactive carbon atom is a carbon atom from an alkyl, acyl or aryl group that will not lead to rearrangement or destruction of the bioactive agent under conditions of ligand exchange during receptor-mediated endocytosis.

5 (Original): The bioconjugate of claim 1, wherein said bioactive agent is covalently bound directly to the cobalt atom of the organocobalt complex.

6 (Original): The bioconjugate of claim 1, wherein said bioactive agent is covalently bound indirectly to the cobalt atom of the organocobalt complex via a spacer.

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7 (Original): The bioconjugate of claim 6, wherein said spacer is a self-destructing linker.

8 (Original): The bioconjugate of claim 1, wherein said bioactive agent is a peptide or peptide analogue.

9 (Original): The bioconjugate of claim 1, wherein said bioactive agent is a protein or protein analogue.

10 (Original): The bioconjugate of claim 1, wherein said bioactive agent is a nucleic acid or a nucleic acid analogue.

11 (Original): The bioconjugate of claim 10, wherein said nucleic acid or nucleic acid analogue is a polynucleotide.

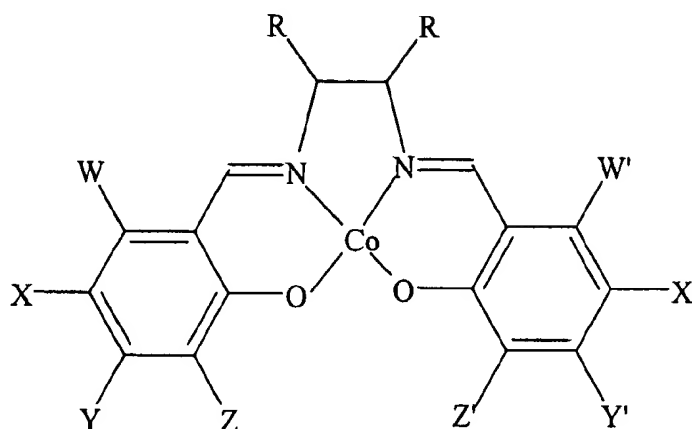
12 (Original): The bioconjugate of claim 10, wherein said nucleic acid or nucleic acid analogue is an oligonucleotide.

13 (Original): The bioconjugate of claim 10, wherein said nucleic acid is antisense DNA or RNA.

14 (Curently amended): The bioconjugate of claim 1, wherein said organocobalt complex is cobalamin, cobalamin lactone, cobalamin lactam, or a cobalamin derivative ~~or a cobalamine analogue~~, wherein said cobalamin derivative is (a) cobalamin in which the benzimidizaole ring is substituted with a halogen, hydroxy or a C<sub>1-6</sub> alkyl, (b) an anilide, ethylamide, monocarboxylic acid, dicarboxylic acid, tricarboxylic acid or propionamide derivative of cobalamin, or (c) cobalamin substituted with an amino, a nitro, a halogen, a sulfito, a C<sub>2-6</sub> alkylene or a C<sub>2-6</sub> alkyne.

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15 (Currently amended): The bioconjugate of claim 1, wherein said organocobalt complex is a compound having the following formula:



wherein

~~the substituents may be included or omitted to modulate physical properties of the molecule, e.g., water solubility, stability of  $\lambda_{max}$  — the wavelength at which the complex absorbs~~ R is H, amino,  $C_{1-6}$  alcohol, or  $C_{1-6}$  carboxyl. W, W', X, X', Y, Y', Z and Z' are independently H, amino,  $C_{1-6}$  alcohol,  $C_{1-6}$  carboxyl,  $SO_3^-$ ,  $CH_2OH$ ,  $CO_2H$ , or nitro, or W and X together form a 4-6 member cyclic or heterocyclic ring, or W' and X' together form a 4-6 member cyclic or heterocyclic ring, or Y and Z together form a 4-6 member cyclic or heterocyclic aromatic ring or Y' and Z' together form a 4-6 member cyclic or heterocyclic aromatic ring.

16 (Currently amended): The bioconjugate of claim 15, which further comprises a targeting molecule covalently linked to one of said R, W, W', X, X', Y, Y', Z or Z', wherein said targeting molecule is selected from the group consisting of glucose, galactose, mannose, mannose 6-phosphate, transferrin, cobalamin, asialoglycoprotein,  $\alpha$ -2-macroglobulins, insulin, a peptide growth factor, folic acid or derivatives, biotin or derivatives, YEE(GalNAcAH)<sub>3</sub> or derivatives, albumin,

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texaphyrin, metallotexaphyrin, a vitamin, a coenzyme, an antibody, an antibody fragment and a single-chain antibody variable region (scFv).

17 (Currently amended): The bioconjugate of claim 1, wherein said organocobalt complex is selected from the group consisting of organo(pyridine)bis(dimethylglyoximato)cobalt, a corrinoid or derivatives thereof and analogues thereof, wherein said derivative is (a) a corrinoid in which the benzimidazole ring is substituted with a halogen, hydroxy or a C<sub>1-6</sub> alkyl, (b) a corrinoid substituted with an amino, a nitro, a halogen, a sulfito, a C<sub>2-6</sub> alkylene or a C<sub>2-6</sub> alkyne, or (c) organo(pyridine)bis(dimethyl-glyoximato)cobalt substituted with an amino, a nitro, a halogen, a sulfito, a C<sub>2-6</sub> alkylene or a C<sub>2-6</sub> alkyne.

18 (Original): The bioconjugate of claim 1, wherein said organocobalt complex comprises a multiple unsaturated heterocyclic ring system bonded to a cobalt atom through 4-5 nitrogens and/or chalcogens which are part of said ring system.